

Ring-opening reactions of benzotriazoles with Wittig reagents

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Dedicated to Professor Dr. Dr. h.c. Michael Hanack on the occasion of his 75th birthday

Abstract—Nonafluorobutanesulfonyl-1*H*-benzotriazole affords phenylazomethylenetriphenylphosphoranes upon treatment with in situ generated alkyl triphenylphosphoranylidenes. Methylenetriphenylphosphorylidene yields the corresponding bis-phenylazo-methylene-triphenylphosphorane.

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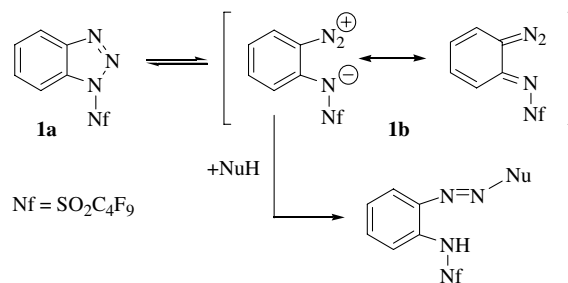
Azomethylene-triphenylphosphoranes are stabilized phosphorus ylides suitable for the synthesis of various heterocyclic compounds. For example, indazolines,¹ cinnolines and oxycinnolines,^{1,2} benzodiazepines,^{3,4} pyrazoles,^{3,5} thia-diazoles,⁶ quinazolines,⁷ and tetrazolium salts^{8,9} have been prepared from azomethylene-triphenylphosphoranes. Such phosphoranes can be prepared either via nitrilimines starting from aryl hydrazonoyl halides^{10–13} or by 1,3-dipolar cycloaddition of nitriloxides, azides, and diazoalkanes to *N*-phenyliminoketenylidene-triphenylphosphorane¹⁴ or by addition of aromatic diazonium salts to Wittig reagents.^{8,15–18} The latter synthesis of azomethylene-triphenylphosphoranes is the most flexible one so far but suffers from the requirement to apply isolated diazonium salts.

Recently, we found that nonafluorobutanesulfonyl-1*H*-benzotriazole **1a** undergoes a clean ring-opening reaction of the triazole moiety upon treatment with carbon nucleophiles. When treated with phenols and naphthols triazole **1a** affords the corresponding azo-arenes.¹⁹ With a broad variety of CH-acidic compounds, **1a** undergoes a Japp–Klingemann reaction yielding the corresponding azo-compounds or hydrazones, respectively, depending on the structure of the applied nucleophile.²⁰ In this sense, nonafluorobutanesulfonyl-1*H*-benzotriazole **1a** reacts like the corresponding diazonium salt **1b**.

Although the precise mechanism of this unusual ring-opening reaction could not be proven unambiguously yet, we speculated that **1a** should react with other nucleophiles via its corresponding diazonium intermediate **1b** as well (Scheme 1).

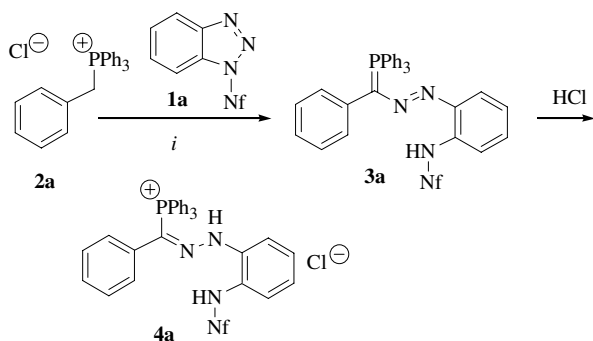
In order to exploit the arenediazonium character of **1a** further, we anticipated its reaction with Wittig reagents via intermediate **1b** to yield the corresponding aryl or alkylazomethylene-triphenylphosphoranes.

Indeed, when benzyltriphenylphosphonium chloride (**2a**) was converted in situ into the corresponding phosphorane and subsequently treated with nonafluorobutanesulfonyl-1*H*-benzotriazole **1a** in THF, tlc indicated a smooth reaction at room temperature, which was completed within 30 min. The initial product **3a** formed from the addition of the Wittig reagent to **1a**



Scheme 1. Reaction of **1a** with nucleophiles via diazonium salt **1b**.

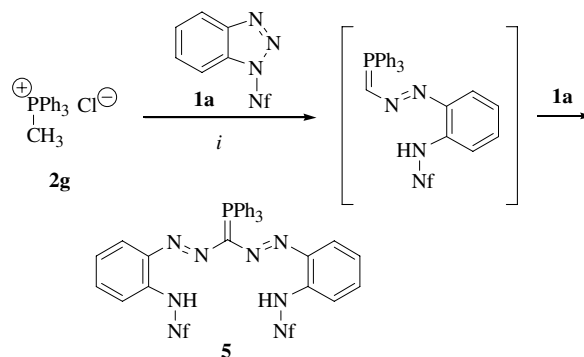
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Scheme 2. Reagents and conditions: (i) (a) 1 equiv **2a**, 1.5 equiv NaH 60% in mineral oil, THF, 25 °C, 4 h; (b) 1.1 equiv **1a**, 25 °C, 0.5 h and (c) HCl_g, EtOAc, 90% **4a**.

was not isolated in this case but treated with HCl and characterized as its triphenylphosphonium chloride **4a** (Scheme 2). It is well known for similar arylazomethylene-triphenylphosphoranes that protonation occurs at the nitrogen of the azo group affording the corresponding hydrazones.^{1,10,15}

Similarly, several other in situ generated Wittig reagents were reacted with **1a** giving the corresponding arylazomethylenetriphenylphosphoranes **3** or their hydrochlorides **4** in medium to good yields (Table 1). The reactions were carried out in THF and the products



Scheme 3. Reagents and conditions: (i) (a) 1 equiv **2g**, 1.5 equiv BuLi in *n*-hexane, THF, 25 °C, 4 h and (b) 2.2 equiv **1a**, 25 °C, 0.5 h, 44% **4**.

were either purified by chromatography or by precipitation as hydrochlorides followed by crystallization.²¹

Reactive methyltriphenylphosphonium bromide **2g** added two molecules of **1a** affording bis-arylazomethylene-triphenylphosphorane **5** in an 44% overall yield (Scheme 3). However, when attempts were made to add ethyl- and isopropyltriphenylphosphonium bromide to **1a**, only an extensive decomposition took place. Obviously, the presence of β-CH groups leads to side reactions and thus, limits this novel preparation of azomethylene-triphenylphosphoranes from benzotriazoles.

Table 1. Reaction of **1** with various triphenylphosphoranes **2**

2	3	Yield (%)
		63
		68
		69
		82
		83

Acknowledgments

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- General procedure*: NaH (1.5 equiv 60% suspension in mineral oil) for phosphonium salts **2a–f** or BuLi (solution in *n*-hexane) for **2g** was added at 25 °C to a solution of **2** in THF and the slurry was stirred for 4 h. Compound **1a**¹⁹ (1.1 equiv for phosphonium salts **2a–f** or 2.2 equiv for **2g**) was added and stirring was continued for 0.5 h. EtOAc and water were added and the aqueous phase was extracted two times with EtOAc. The combined organic extracts were dried with sodium sulfate, filtered, and evaporated. The chromatography of the residue on silica gel with EtOAc afforded compounds **3** and **5**, respectively. In the case of compounds **3a** and **3b**, dry HCl was bubbled through the dried solution of the crude products in EtOAc, the solvent and excess HCl were evaporated and the residue crystallized from a small amount of EtOAc to give **4a** and **4b**, respectively. All compounds gave satisfactory elemental analysis results. Compound **4a**: mp 213–214 °C (dec.). IR (KBr): 3437 (NH), 1349, 1192 (SO₂), 1439 (CP), 1266, 1033 cm⁻¹ (CF). UV/vis (CH₃CN): λ = 328 nm (8540). ¹H NMR (250 MHz, CDCl₃): δ = 6.86–6.97 (m, 2H, H-4, H-6), 7.00–7.07 (m, 1H, H-5), 7.12–7.16 (m, 2H, H-3', H-5'), 7.29 (dd, 1H, J₃₋₄ = 1.5, J₃₋₅ = 7.6 Hz, H-3), 7.33–7.42 (m, 3H, H-2', H-4', H-6'), 7.47–7.65 (m, 12H, H-2'', H-3'', H-5'', H-6''), 7.76–7.84 (m, 3H, H-4''), 10.72 (s, 1H, NH). ¹³C NMR (62.9 MHz, CDCl₃): δ = 116.5 (C-6), 118.7 (d, J_{1''-P} = 89.6 Hz, C-1''), 122.9 (C-1), 124.0 (C-4), 125.7 (d, J_{CP-P} = 130 Hz, C-CP), 127.4 (d, J_{1'-P} = 20.3 Hz, C-1'), 128.3 (C-5), 129.9 (C-4'), 130.1 (C-3', C-5'), 130.1 (d, J_{2''-P/6''-P} = 12.2 Hz, C-2'', C-6''), 130.2 (C-3), 131.4 (d, J_{2'-P/6'-P} = 1.74 Hz, C-2', C-6'), 134.4 (d, J_{3''-P/5''-P} = 9.6 Hz, C-3'', C-5''), 135.1 (d, J_{4''-P} = 3.5 Hz, C-4''), 138.5 (C-2). FAB-MS: m/z = 754.14 [M+H]⁺. Compound **4b**: mp 206–208 °C (dec.). IR (KBr): 3425 (NH), 1192 (SO₂), 1439 (CP), 1348 (NO₂), 1268, 1131, 1032 cm⁻¹ (CF). UV/vis (CH₃CN): λ = 317 nm (16,100). ¹H NMR (250 MHz, CDCl₃): δ = 6.64–6.71 (m, 1H, H-5), 6.80–6.87 (m, 2H, H-4, H-6), 7.20–7.24 (m, 2H, H-2', H-6'), 7.38–7.42 (m, 1H, H-3), 7.51–7.68 (m, 12H, H-2'', H-3'', H-5'', H-6''), 7.77–7.85 (m, 3H, H-4''), 8.09–8.12 (m, 2H, H-3', H-5'), 10.62 (s, 1H, NH). ¹³C NMR (62.9 MHz, CDCl₃): δ = 112.7 (C-6), 116.9 (d, J_{CP-P} = 137.6 Hz, C-CP), 118.8 (d, J_{1''-P} = 90.5 Hz, C-1''), 120.9 (C-5), 123.9 (C-3), 124.9 (C-4), 125.3 (C-3', C-5'), 130.3 (d, J_{2''-P/6''-P} = 12.9 Hz, C-2'', C-6''), 130.9 (d, J_{2'-P/6'-P} = 3.2 Hz, C-2', C-6'), 133.7 (C-1), 134.3 (d, J_{3''-P/5''-P} = 9.7 Hz, C-3'', C-5''), 134.4 (d, J_{1'-P} = 21.7 Hz, C-1'), 135.3 (d, J_{4''-P} = 3.23 Hz, C-4''), 135.9 (C-2). FAB-MS: m/z = 799.1 [M+H]⁺. Compound **3c**: mp 199–200 °C (dec.; EtOAc). IR (KBr): 3425 (NH), 1350, 1192 (SO₂), 1439 (CP), 1265, 1130, 1030 cm⁻¹ (CF). UV/vis (CH₃CN): λ = 379 nm (5410). ¹H NMR (250 MHz, CDCl₃): δ = 6.63–6.68 (m, 1H, H-5), 6.75–6.89 (m, 3H, H-4, H-6, H-2'), 7.09–7.11 (m, 1H, H-6'), 7.35–7.37 (m, 2H, H-4', H-5'), 7.48–7.67 (m, 13H, H-3, H-1'', H-2'', H-3'', H-4''), 7.78–7.84 (m, 3H, H-4''), 10.6 (s, 1H, NH). ¹³C NMR (62.9 MHz, CDCl₃): δ = 112.4 (C-6), 117.5 (d, J_{CP-P} = 137 Hz, C-CP), 119.1 (d, J_{1''-P} = 90.5 Hz, C-1''), 120.5 (C-5), 123.7 (C-3), 124.6 (C-4), 127.9 (d, J_{6'-P} = 4.2 Hz, C-6'), 129.3 (d, J_{1''-P} = 21.7 Hz, C-1'), 129.6 (d, J_{2'-P} = 2.8 Hz, C-2'), 130.1 (d, J_{2''-P/6''-P} = 12.9 Hz, C-2'', C-6''), 131.2 (d, J_{5'-P} = 1.4 Hz, C-5'), 131.8 (C-4'), 133.8 (C-1), 134.25 (d, J_{3''-P/5''-P} = 10.2 Hz, C-3'', C-5''), 135.1 (d, J_{4''-P} = 3.2 Hz, C-4''), 136.0 (C-3'), 136.2 (d, J_{2'-P} = 1 Hz, C-2). FAB-MS: m/z = 788.0 [M+H]⁺. Compound **3d**: mp 200–203 °C (dec.; EtOAc). IR (KBr): ν = 3442 (NH), 1350, 1190 (SO₂), 1439 (CP), 1267, 1029 cm⁻¹ (CF). UV/vis (CH₃CN): 379 nm (5480). ¹H NMR (250 MHz, CDCl₃): δ = 6.62–6.69 (m, 1H, H-5), 6.77–6.88 (m, 2H, H-4, H-6), 6.95 (d, 2H, J_{2'-3'/6'-5'} = 8.3 Hz, H-2', H-6'), 7.30 (d, 2H, J_{3'-2'/5'-6'} = 8.3 Hz, H-3', H-5'), 7.45–7.66 (m, 13H, H-3, H-2'', H-3'', H-4'', H-6''), 7.77–7.84 (m, 3H, H-4''), 10.49 (s, 1H, NH). ¹³C NMR (62.9 MHz, CDCl₃): δ = 112.5 (C-6), 118.1 (d, J_{CP-P} = 137 Hz, C-CP), 119.2 (d, J_{1''-P} = 89.8 Hz, C-1''), 120.6 (C-5), 123.9 (C-3), 124.4 (C-4), 126.0 (d, J_{1'-P} = 21.7 Hz, C-1'), 130.1 (d, J_{2''-P/6''-P} = 12.9 Hz, C-2'', C-6''), 130.7 (C-3', C-5'), 130.9 (d, J_{2'-P/6'-P} = 3.7 Hz, C-2', C-6'), 133.9 (C-1), 134.3 (d, J_{3''-P/5''-P} = 10.2 Hz, C-3'', C-5''), 135.1 (d, J_{4''-P} = 2.8 Hz, C-4''), 135.8 (C-4'), 137.3 (d, J_{2'-P} = 1.9 Hz, C-2'). FAB-MS: m/z = 788.0 [M+H]⁺. Compound **3e**: mp 208–209 °C (dec.; EtOAc). IR (KBr): 3445 (NH), 1192 (SO₂), 1440 (CP), 2843 (OMe), 1264, 1133, 1033 cm⁻¹ (CF). UV/vis (CH₃CN): λ = 374 nm (7690). ¹H NMR (250 MHz, CDCl₃): δ = 3.74 (s, 3H, H-CH₃), 6.61–6.68 (m, 1H, H-5), 6.77–6.94 (m, 6H, H-4, H-6, H-2', H-3', H-5', H-6'), 7.45–7.64 (m, 13H, H-3, H-2'', H-3'', H-5'', H-6''), 7.74–7.82 (m, 3H, H-4''), 12.45 (s, 1H, NH). ¹³C NMR (62.9 MHz, CDCl₃): δ = 55.3

(CH₃), 112.4 (C-6), 115.9 (C-3', C-5'), 119.2 (d, $J_{1'-P} = 21.7$ Hz, C-1'), 119.5 (d, $J_{1''-P} = 89.6$ Hz, C-1''), 119.9 (d, $J_{CP-P} = 134$ Hz, C-CP), 123.8 (C-3), 123.9 (C-4), 130.0 (d, $J_{2''-P/6''-P} = 12.5$ Hz, C-2'', C-6''), 131.1 (d, $J = 3.7$ Hz, C-2', C-6'), 134.3 (d, $J_{3''-P/5''-P} = 9.7$ Hz, C-3'', C-5''), 134.3 (C-1), 134.9 (d, $J_{4''-P} = 2.8$ Hz, C-4''), 135.3 (C-2), 161.4 (C-4'). FAB-MS: $m/z = 784.0$ [M+H]⁺. Compound **3f**: mp 194–197 °C (dec.; EtOAc). IR (KBr): 3442 (NH), 1349, 1191 (SO₂), 1688 (CO), 1440 (CP), 1264, 1130, 1029 cm⁻¹ (CF). UV/vis (CH₃CN): 410 nm (13,400). ¹H NMR (250 MHz, CDCl₃): $\delta = 1.09$ (t, 3H, $J_{1''-2''} = 7.1$ Hz, CH₃), 4.29 (q, 2H, $J_{2''-1''} = 7.1$ Hz, CH₂) 6.55–6.58 (m, 2H, H-3, H-4), 6.92–6.99 (m, 1H, H-5), 6.55–6.58 (m, 2H, H-3, H-4), 7.58–7.70 (m, 13H, H-6, H-2', H-3', H-5', H-6'), 7.76–7.84 (m, 3H, H-4'), 13.89 (s, 1H, NH). ¹³C NMR (62.9 MHz, CDCl₃): $\delta = 13.9$ (C2''-CH₃), 62.9 (C1''-CH₂), 104.5 (d, $J_{CP-P} = 145$ Hz, C-CP), 113.4 (C-3), 119.7 (d, $J_{1'-P} = 93.26$, C-1'), 120.0 (C-4), 122.7 (C-6), 127.5

(C-5), 129.8 (d, $J_{2'-P/6'-P} = 12.9$ Hz, C-2', C-6'), 133.0 (C-2), 134.1 (d, $J_{3'-P/5'-P} = 10.2$ Hz, C-3', C-5'), 134.6 (d, $J_{4'-P} = 2.8$ Hz, C-4'), 138.7 (C-1), 161.6 (d, $J_{CO-P} = 27.2$ Hz, C-CO). FAB-MS: $m/z = 749.9$ [M+H]⁺. Compound **5**: mp 190–193 °C (petroleum ether/EtOAc). IR (KBr): 3442 (NH, OH), 1350, 1191 (SO₂), 1440 (CP), 1134, 1035 cm⁻¹ (CF). UV/vis (CH₃CN): 534 nm (12,800). ¹H NMR (250 MHz, CDCl₃): $\delta = 6.89$ –6.95 (m, 2H, H-4, H-4'), 7.02–7.06 (m, 2H, H-3, H-3'), 7.09–7.16 (m, 2H, H-5, H-5'), 7.45–7.48 (m, 2H, H-6, H-6'), 7.59–7.67 (m, 12H, H-2'', H-3'', H-5'', H-6''), 7.71–7.81 (m, 3H, H-4''), 16.5 (s, 2H, NH). ¹³C NMR (62.9 MHz, CDCl₃): $\delta = 115.8$ (C-3, C-3'), 119.1 (d, $J_{1''-P} = 92.3$ Hz, C-1''), 125.1 (C-4, C-4'), 126.6 (C-6, C-6'), 128.0 (d, $J_{CP-P} = 174$ Hz, C-CP), 130.0 (d, $J_{2''-P/6''-P} = 12.9$ Hz, C-2'', C-6''), 130.5 (C-5, C-5'), 134.2 (d, $J_{3''-P/5''-P} = 10.2$ Hz, C-3'', C-5''), 134.9 (C-2, C-2'), 135.1 (d, $J_{4''-P} = 3.2$ Hz, C-4''), 140.8 (C-1, C-1'). FAB-MS: $m/z = 1078.9$ [M+H]⁺.